TITLE: OPHTHALMIC MANIFESTATIONS OF SEXUALLY TRANSMITTED DISEASES-KEY DIAGNOSTIC INDICATORS TO SUGGEST GONOCOCCAL AND CHLAMYDYDIAL OCULAR DISEASE

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[video transcript]

[00:00:07] I'm going to talk today about gonococcal and chlamydial ocular disease. And I don't have any relevant financial relationships. We'll skip the learning objectives and just get right to it. Gonococcal Conjunctivitis, I defined it here as a highly dangerous, hyper acute, that's the classic word to describe this, conjunctivitis caused by neisseria gonorrhea, which if untreated may lead to vision threatening ocular complications. And we all know, we've all seen this slide, I'm sure, showing intercellular gonococcal organisms, diplococci, gram-negative in PMN's or neutrophils, certain type of white blood cell. I have a tiny arrow arrow there that you may have trouble seeing showing, you can see the darker nucleus in each cell, the multi-lobed nucleus, and then the small circles are the diplococci. Now in the course of making sure that what I was presenting was correct, I came across this on Etsy. I don't know if you guys know what Etsy is, but someone seems to have made a hobby out of making cable covers and wall covers with that slide. So, everybody has their own little thing I guess. OK. So, GC infects endocervix, urethra, anogenital mucous membranes, oropharyngeal mucous membranes, and can affect the conjunctiva. It is always considered pathogenic when identified. It's a lot of cases almost a million a year. The majority of the infections in men produce symptoms. Those in women typically don't. The infection may not, it can last a long time especially in women. The incubation period is from three to nineteen days and in terms of diagnosis it gets a little into what we talked about before.

[00:02:04] We need some sort of microbiologic diagnosis which can be anything from a gram stain, to a culture, to NAAT, to other types of DNA and other probes. And having a specific diagnosis in this case in these cases for us is very helpful. It's obviously helpful to you in terms of complications and reinfections and transmission, but we treat this sort of conjunctivitis very different than any other sort of conjunctivitis. So, you can do a gram stain from urethral specimens in males, a negative doesn't rule it out. It's not on and females typically. The NAAT is the gold standard. There are reasons the culture is particularly helpful when the clinical diagnosis is unclear, when treatment failures occurred. If contact tracing is problematic or if there are legal questions. Typically you want to do a direct inoculation on to Chocolate AGAR, Thayer-Martin AGAR as opposed to sending just a general transport media. So, the nucleic acid with occasional tests. That's the gold standard, it has the highest sensitivity and specificity, ease of transport, widest variety of FDA cleared specimen types, and this gets into a little bit of what's approved. So, urethral swabs are approved, cervical swabs, urine self-collected vaginal swabs. It's not approved for rectal and pharyngeal or conjunctiva, although I think it's generally considered to be an excellent test for all three. I've never gotten one I just haven't seen enough to have been in that situation. And I'm not sure what they use at the hospital here, some of the NAATS can be used for both chlamydia and gonorrhea. And we have that here?

[00:04:00] Yes
So, let's talk about conjunctivitis and this is really this is we're getting to the good part. Conjunctivitis in general, not specifically to GC, is a conjunctival inflammatory disease which affects the conjunctiva primarily. It's classically infectious, but it doesn't have to be. Patients come in with a red eye and, almost by definition, that's conjunctivitis, but it can be autoimmune, or allergic, or traumatic. There can be other things. For the classically infectious, you know be it staph or something like that, they're usually self limited and we don't get too excited about them; we put patients on antibiotics and they get better. But they don't typically progress to other deeper ocular complications. And what we typically use as outcome criteria are to eliminate or reduce signs and symptoms of the conjunctivitis, to get back the vision, to treat any underlying disease process when applicable, and prevent, reduce likelihood of damage to the ocular surface. These things kind of just happen from most types of conjunctivitis and we usually throw a non-specific treatment, usually go with polytrim, which is trimethoprim, or we go with vigamox, which is a fluoroquinolone, and they get better. We don't even follow them up for the most part. So, the conjunctiva is just to make sure we're all on the same page here. There's two kinds of conjunctiva, there is conjunctiva where, can you see the purple we're where it's over the white of the eye?

The entire white the eyes cover with conjunctiva, and the conjunctiva is a clear spongy layer, and it stops at the limbus. The limbus is the area where the cornea starts. So, the cornea is like the watch glass on the surface that you're looking through when you when you look at the pupil when you look at the iris, you're looking through the clear cornea and you don't typically see the conjunctiva because you're seeing the white sclera through the conjunctiva. So, one of the types of conjunctiva is Bulbar Conjunctiva and it's called that because it's on the bulb, it's on the globe, it's on the eye. And then the conjunctiva continues up the back of the lids and so in the picture on your left the lid is being pulled down and that's called the palpebral conjunctiva, and the conjunctiva can show things like white blood cells collecting there, it can show redness, it can show vascular injection and congestion, it can show swelling. And so, on you're right, when you look at that picture and you see this red eye, you're really not seeing the sclera as red, you're seeing the clear conjunctiva with now dilated blood vessels which take on this red or pinkish hue. And the cornea is clear and you can tell it's clear because when we looked through the cornea you can see the iris and the pupil fairly easily. So, that's sort of conjunctivitis in general and the parts of the eye. Let's talk now about GC conjunctivitis. Now we're getting close to the good stuff. Urethral symptoms precede the ocular symptoms by one to several weeks. It's usually the result of auto-inoculation. And I'm going to show you photos of all these. But just as a kind of quick summary it can be unilateral or bilateral. It's hyper-acute and it's the only conjunctivitis that is considered to be hyper-acute and by hyper-acute we mean stormy onset, pus, redness, miserable you know just it kind of tells you that it's that it's GC.

It's one of the few that give you marked eyelid edema and that's what gets mistaken for preseptal or orbital cellulitis. You can have marked bulbar conjunctiva injection and marked palpebral conjunctival injection. And the biggest thing, the thing that's most easily noticed, is marked purulent discharge, there's just pus everywhere. Now preauricular lymphadenopathy, that's right in front of the
ear, there's a lymph node that typically only gets dilate, enlarged for viral infections or chlamydia. This is one of the few bacteria with chlamydia that cause an enlarged preauricular lymph node. So, whenever we're trying to rule out a viral conjunctivitis or even herpes, the first thing we do is we go and look and see if that lymph node is swollen and tender. You do see that in gonococcal conjunctivitis. So, right away, when you have a preauricular lymph node, and you have a purulent conjunctivitis, you're already in the GC, you know, sort area being suspicious. Chemosis is when fluid collects beneath the bulbar conjunctiva and you get a lot of swelling and you can have really intense dilation of the conjunctival vessels so that he can see the white of the eye. The only published study that I know of was from 1989 that talked about treatment. All 12 patients responded to a single IM injection of Ceftriaxone. There is rationale for using Zithromax not just a cover chlamydia but also as a second antibiotic for GC. We, in the few times that we see this, we typically get an ID consult to make sure we're doing the right thing.

[00:09:11] And the treatment, according to the CDC 2015 recommendations for adult and adolescence conjunctivitis, the 1 gram single dose Ceftriaxone and Zithromax. And I just, for your perusal, I just a different chart that's a little easier to read for you. OK, so treatment. Topical, the eye itself. Saline lavage, just get that pus out of there because that puss is really toxic to the surface. There are lytic enzymes in it, and so basically you just try to keep the eye clean. Sometimes we'll use antibiotics, but our typical antibiotics don't work. You can do intensive fortified antibiotics, compounded medications, penicillin G, but it doesn't work that well either. But, maybe putting antibiotics on top of the eye is helpful, maybe not there aren't good studies that really look at it, but we tend to do that. And, in terms of treatment resistance, the only reason I put this in there is that our, the typical antibiotics that we use, don't cover GC very well. Being fluoroquinolones and polytrim. This is an example of a stormy onset of conjunctivitis where we have pus sort of coming from the eye, coating the lids, coating the lashes, as soon as you remove this there's more that comes within minutes. Here the cornea which, is black, is clear, it's because of the lighting that you're not really seeing through it, but we do see a lot of swelling on the eye itself which is fluid collecting beneath the conjunctiva; the conjunctiva intensely red and a very stormy onset.

[00:11:04] So, in these kinds of cases, we're trying to rule out sort of two sets of issues. One is, because of the lid edema, there's an overlap with preseptal cellulitis and orbital cellulitis, and in terms of conjunctivitis, we're ruling out other less virulent organisms in terms of causing this. But when you see this much pus, I mean this really you know you have to be suspicious for GC. I'm trying to change and I'm not getting it. So, can we, is there a way to, there we go. OK. So, here what we see is the lower lid being pulled down. And so you can see the conjunctiva on the inside of the lower lid, it reflects down in the fornix, sort of inside, and then it goes up the eye, and then it stops where the cornea starts. And all of the white that you're seeing there is pus coating the surface and if you remove this pus with a Q-tip, again five or ten minutes later, you'll see the post there again. So, we have intense injection of the conjunctiva and a very pusy eye. Here's another case where the lower lid is being pulled down. You can see swelling on the inside of the lower lid, swelling as you go forward under the as you go up, I'm sorry, under the bulbar conjunctiva, intense redness and swelling, and copious pus. Now at this point the
vision will be down because pus is covering the cornea and you have to be able to distinguish between the vision being down because there's a corneal problem and because you're looking through all this copious pus. Another picture of here we have on your right bleeding. So, you can see on your right the conjunctiva, the redness there, is a little bit different. On the left, you can actually see the blood vessels. On the right,

[00:13:02] all you see is red. And that is one of the things that can happen when the conjunctivitis is severe, can get bleeding. And again you can see all the pus down below and up above on the lashes. This is the problem. So, it's not the conjunctivitis itself that's so worrisome, it's the fact that this conjunctivitis can turn into a keratitis. A keratitis refers to an inflammation, and in this case infection, of the cornea. And when that happens the cornea can perforate due to melting of the cornea itself in under 24 hours. And so, if that happens, if you don't lose the eye immediately, at very least you require corneal grafting where you replace the cornea. This can happen you know between the time you send the patient out and the next day. Prompt diagnosis and treatment are essential. There are no other forms of conjunctivitis that go on to do this. The degree of corneal involvement is variable. It can be in the center, it could be in the periphery, you can have melting at the limbus close to the Sclera, you're going to have white blood cell collections within the cornea where it doesn't melt, the whole cornea it could be edematous, and it could also be accompanied by other types of inflammation in the eye, primarily the iris. So, these are pictures, and I hope they're coming out because you have to, you have to look a little bit closely, we have a cornea here that is white on the top, you can barely even make it out as a cornea. And if you looked in the center of your screen there's a sort of a black area on the top of the cornea.

[00:14:44] And what that is is the cornea has been infected, it's melted, there's a hole in the cornea, and the iris, the color part, has come up and out the cornea. So, it's not lost from the cornea, but it's plugging the hole in this case. And this kind of thing can happen overnight. Again, we see all the hemorrhages, we see all the the white blood cells in the cornea. This is a little less fulminant. But again, when you see a dark spot in the cornea like that that is a hole in the cornea which is plugged with iris. Now, in this case here it's so fulminant. If you patch that up, you really, it's a tough go because when you patch it up you're sewing cornea on top of if and there's not a whole lot to sew to. But something like this is pretty easy to fix. And having the iris plug the whole is actually a good thing it keeps everything kind of where it should be. And then we would go in and push the iris back and do a limited corneal transplant where we use human tissue to replace the cornea in the region that has melted. But, this is the only type of conjunctivitis that can lead to this. So, hence, you know it's differentiation from all other forms of conjunctival infection. Another cornea you can see the white. In the middle, it may seem like it's doing better but it's because the cornea has been lost; there's just no cornea there, it's just soup. The dark side here is not iris, that's just, you know, you're looking through into the eye and it's just the way the lighting is.
[00:16:16] You can see some hemorrhages sort of in that soupy mess. And I apologize for the grossness but that's GC, I mean, that's why we take it so seriously. So, here's a happy ending. Here we have the top. We have and ulcer. We have an ulcer that perforated in B. These are not my slides, but it's a good example. Here we have a corneal transplant in C, where we took a piece of cornea sewed over the area of perforation. And in D, we have a cornea several months out where everything's back to normal. And so that's why we watch these people so closely. Another ulcer, this is an example of a hypopyon, where inside the eye there's pus forming behind the cornea and actually settling out down below. And then the cornea itself is infected up above with some melting an severe injection infection. Think you’re getting the feel here. This was an especially bad one, a very large corneal perforation. A lot of different looks. And here's a corneal transplant, here's a full circular corneal transplant. You can see the sutures. There's two sets of sutures here, interrupted sutures, individual sutures, as well as, a running suture, like a hem stitch. And, you know, if you’re on top of things, patients do well. Okay, so I'm done with GC, and I took longer than I had expected. Should I just keep lecturing?

[00:18:00] Yes.

[00:18:01] Okay, I'd like to talk to you about chlamydia. So, the severity of this, in terms of ophthalmology in the eyes, is very different.

[00:18:13] For us, it really becomes more of a mystery when a patient comes in with a type of conjunctivitis, we're always thinking is it chlamydia. And this we see not infrequently. So, quickly, sexually transmitted requires host cell for invasion, intercellular growth, and replication. So, it kind of acts like a virus. Passed along the same way as for GC. Likewise, symptoms are more common men than women. It's the chlamydia trachomatis is what the species that causes the eye disease, it also causes most of the disease that you deal with, the others are pneumonia and psittaci and there are certain stereotypes associated with each one of these things; for adult inclusion conjunctivitis, it's serotype D through K. So, every ophthalmology resident knows this. That's D through K. In terms of the life cycle, it makes a good picture of the teeny tiny little purple dots are released from the cell which are the elementary bodies that are the chlamydia, the infectious element. They're then taken into the cell, on your upper right the elementary bodies get turned into reticulate bodies, which are intracytoplasmic forms, and then they kind of bound together and they form an inclusion. And when you see the pathology, you'll see an inclusion adjacent to the nucleus with these, which are showing a moment. These mature to form elementary bodies and then the elementary bodies are released from the cell. And in the upper right, I have an arrow pointing to the vacuole, the inclusion body that is diagnostic and characteristic of chlamydia. And then the bottom, we have labeled elementary bodies which are free at this point, which are infectious particles. So, for men we have urethritis, proctitis, and conjunctivitis, women similar, infants can also get a pneumonitis.
In terms of testing, we have the nucleic acid amplification test. And we rarely do any culturing for this, because if patients come in with a certain set of signs, we typically treat empirically were the few things that can look alike are all treated by doxy or zithromycin. So, for instance, chlamydia and cat scratch disease, which can look very much alike when we see both fairly frequently, the treatments the same. And so, we don't end up typically doing cultures or any kind of immunofluorescent tests. Right. So, let's get to the good stuff here. The actual conjunctivitis. Not nearly as gross. It happens one to two weeks after ocular inoculation, it's usually auto-inoculation; 40 to 90 percent also have genital chlamydia. The infected conjunctival epithelial cells do contain these inclusion bodies. Repeat infection can lead to scarring, but it doesn't typically. There is a triad of arthritis, conjunctivitis, and urethritis, which can occur with chlamydia. And typically this is self limited, I mean the patients are kind of miserable but it doesn't do anything particularly bad. So, here, not hyper-acute; it can be unilateral bilateral. You can get redness and it can be quite severe, but it's not beefy. You can get what's called a papillary reaction where you get bumps on the conjunctiva, which I'll show, and you can get a follicular reaction where you actually have clumps of white blood cells collecting in the conjunctiva. The discharge is scant as opposed to GC and you get a little eyelid swelling. And again, your other bacteria that can cause Pre-auricular adenopathy. And no membranes form in the eye the way they do with other things like contagious pinkeye.

And the virus. So, here we have the lower lid being pulled down and you can see the upper lid and you can see the light reflexes just the little dots of light. And those those are bouncing off of individual little mounds of white blood cells and areas of injection. And it's very typical for chlamydia. And on your right, we have the two different kinds of swellings. On the arrow on your right, is pointing to sort of a milky white swelling, those are, it's kind of like a lymph node, I mean they're swellings of collected white blood cells. And on your left, also actually, I initially thought that was a papillary reaction, but I think those are follicles as well. Those, they're sort of whitish and anything kind of whitish is a collection of white blood cells. And again, just some some larger views of what these collections, these dots, these small little collections look like. You can see it maybe a little better and you're right where they're kind of formed in a line and that's in the lower fornix, that's the lower lid being pulled down. And so they're not really on the eye, on the bulbar conjunctiva here, these are on the help palpebral conjunctiva.

I just needed to show you what the cornea is. The cornea is the watch glass that you’re looking through. On the lower left, we see sort of a patient looking straight up where you can see the colored iris, and you can see the cornea. And you can’t really see the cornea when you look at it with a picture, but you can see any opacity in the cornea, you can see whiteness and the cornea, or you may see it as not being able to see the colored iris very well. But it's hard to see the cornea itself, but I’m gonna try to show you some pictures. The cornea, there's a lot of findings. They all have, you know, fancy names but the bottom line is that it does two things. It forms blood vessels come, the first blood vessels up top, which come from the conjunctiva. And you can see here they're growing down onto the cornea and below, the two arrows below, are areas of collected inflammation, and that inflammation
pulls in the vessels; there are cytokines and chemotactic factors that that pull inflammation in and part of that inflammation are those blood vessels coming down. So, when we see a follicular reaction down below, on the conjunctiva, and blood vessels up above like this, this is pretty classic for chlamydia and this can be seen in untreated chlamydia. But notice it doesn't really involve the center very much. Yes, some of the white blood cells, but the vessels are coming from the conjunctiva area. They got a long way to go to get to the center. So, in the upper picture, again, we have some white spots on the cornea which is inflammation. In the lower left, we have inflammation in the peripheral cornea.

[00:25:18] And those are not vision threatening at all because they pull in inflammation, but it's just pulling it to where the inflammation is. And so you get vessels but they don't go towards the center. And on the right, we have there's two arrows I have on the right picture. The first on the upper arrow is just the white bloods, the I'm sorry, the vessels in the bottom as you can see little pockets of white blood cells which are pulling the vessels in. Another thing that can happen is you can affect, be toxic to the surface. And what the surface looks like here in the epithelium, it's a layer that reproduces itself, a we don't get too excited about it, but if you have a bowl of jello and took a piece of sandpaper and touched the jello, that's what the surface looks like and we put that yellow dye in and you don't see an abrasion the way you might use that yellow dye in an ED, here we see all these little dots and that affects the vision, but it's not permanent. This is untreated chlamydia, where those white spots have sort of entrenched. There is actually opacity, and this could be a little vision threatening, but this is not typical. Again peripheral areas of white blood cell collection where I have the arrows in untreated chlamydia. And the treatment is either doxy or azithromycin. And I have just a copy from the 2015 CDC.

[end]